The Lancet Digital Health Publishes Akili AKL-T01 ADHD Pivotal Study Results

February 24, 2020

First publication of complete results shows improvement across both objective measures of attention and parent and clinician ratings of ADHD symptoms and functional impairments

Study results suggest AKL-T01 could play an important role in the treatment of paediatric ADHD, directly targeting attention impairments

PureTech Health plc (LSE: PRTC) ("PureTech") is pleased to note that its affiliate, Akili, has published the results from its *STARS-ADHD* trial of AKL-T01, a digital therapeutic designed to improve attention in children with attention-deficit/hyperactivity disorder (ADHD), in The Lancet Digital Health journal. The publication represents the first presentation of complete results from the *STARS-ADHD* trial, a first-of-its-kind large, randomised, multi-centre, controlled study of the company's foundational technology and the first seminal trial in a series of recent and ongoing studies of the attentional treatment. Results show AKL-T01 improved both objective measures and parent observations of attention and functional impairments.

Eric Elenko, PhD, chief innovation officer at PureTech, said: "These complete results provide compelling insights and further validation for AKL-T01 for the treatment of inattention in children with ADHD. It also builds on the recently reported findings from Akili's *STARS-ADHD* Adjunctive study, which demonstrated additional promise for AKL-T01 as both a monotherapy and in combination with stimulant medications. It is exciting to see the mounting data for AKL-T01 which validates its potential."

The *STARS-ADHD* study represents the company's largest clinical trial of AKL-T01 which has to-date been studied across five clinical trials including more than 600 children diagnosed with the disorder. Further researching the clinical implications of the attentional treatment on patients' daily lives, Akili recently conducted the *STARS-ADHD* Adjunctive study evaluating AKL-T01 in children with ADHD when used with and without stimulant medication as well as evaluating the effects of increasing the duration of AKL-T01 treatment. In the *STARS-ADHD* Adjunctive study, AKL-T01 showed a statistically significant improvement in the Impairment Rating Scale (IRS) when used alone and as adjunct to stimulants, and parents and clinicians saw increased improvements with a longer duration of AKL-T01 treatment (nearly 70% saw improvements after two months of treatment). Additional studies of AKL-T01 are underway, including a study to measure frontal-midline theta (MFT) power through electroencephalogram (EEG) in children with ADHD before and after treatment with AKL-T01.

The full text of the announcement from Akili is as follows:

Akili Announces Publication of AKL-T01 ADHD Pivotal Study Results in The Lancet Digital Health

First publication of complete results shows improvement across both objective measures of attention and parent and clinician ratings of ADHD symptoms and functional impairments

Study results suggest AKL-T01 could play an important role in the treatment of paediatric ADHD, directly targeting attention impairments

BOSTON, Mass – February 24, 2020 – Akili Interactive today announced that results from the *STARS-ADHD* trial of AKL-T01, a digital therapeutic designed to improve attention in children with attention-deficit/hyperactivity disorder (ADHD), were published in The Lancet Digital Health journal. The publication represents the first presentation of complete results from the *STARS-ADHD* trial, a first-of-its-kind large, randomised, multi-centre, controlled study of the company's flagship technology and the first seminal trial in a series of recent and ongoing studies of the attentional treatment. Results show AKL-T01 improved both objective measures and parent observations of attention and functional impairments.

ADHD is a disorder marked by a persistent pattern of inattention and/or hyperactivity-impulsivity that interferes with functioning or development. Inattention is a key component of ADHD for many children and can significantly impact daily functioning. However, inattention and other "silent" cognitive issues often go unrecognised in the face of other more overt disease symptoms.

"For children living with ADHD, inattention can lead to significant impairments across domains, including school performance, home life and interpersonal relationships, yet it is often overshadowed by the more overt symptoms of the disorder and is often not optimally addressed by standard treatments," said Dr Scott Kollins, Professor of Psychiatry, Director of the ADHD Program at Duke University School of Medicine, who was the Duke Clinical Research Institute principal investigator on the study. "Products that can specifically improve a child's inattention could represent safe and easy to access interventions that have the potential to play an important role in the overall treatment of ADHD."

In the study of 348 children diagnosed with ADHD, AKL-T01 showed improvements across a wide range of attention measures, from objective measures of attention to how attention impacted daily life and functioning. AKL-T01 showed a statistically significant improvement compared to an educational-style video game control (p=0.006) on the predefined primary endpoint, a change in the Attention Performance Index (API) of the Test of Variables of Attention (TOVA®). TOVA is a computerised test cleared by the US Food and Drug Administration (FDA) to assess attention deficits and evaluate the effects of interventions in ADHD. The mean (SD) change from baseline on the TOVA API (a composite measure of attention functioning) was 0.93 in the AKL-T01 group and 0.03 in the control group. Forty-seven percent of children met the prespecified clinical responder analysis for TOVA API improvement, which was greater than control (47% vs 32%, p=0.0058). In addition to the improvement in the TOVA API, treatment with AKL-T01 resulted in significantly greater improvements across other objective TOVA attention-related measures (sustained attention, attentional consistency, and long attentional lapses). Overall, after treatment with AKL-T01, 36% of children moved into the normative range and no longer showed an attention deficit in at least one aspect of attention functioning, statistically greater than control (36% vs 21%, P=0.0027).

In addition to these objective measures of attention, the study also looked at secondary outcome measures comparing AKL-T01 to control on parent- and clinician-reported ADHD impairment and symptom ratings scales, including the Impairment Rating Scale (IRS), ADHD Rating Scale (ADHD-RS-IV - Total, Inattentive, Hyperactive subscales), Clinical Global Impressions-Improvement (CGI-I) and the Behavior Rating Inventory of Executive Function (BRIEF). Children using AKL-T01 showed statistically significant improvement across all measures. Though there was not a statistically significant

separation on the mean magnitude of effect between AKL-T01 and control, there was a trend towards differential improvement in IRS and ADHD-RS-Inattentive for children using AKL-T01.

Responder analyses of these parent- and clinician-reported measures showed a significantly greater proportion of children benefiting from AKL-T01 versus control in the IRS, a parent-reported scale of ADHD-specific impairments, (48% vs 37%, P=0·049). Additionally, 56% of parents said the intervention helped their child's attention in real life, and 73% of children reported feeling an improvement in their attention when asked via an exit survey. Analysis of the full set of responder analyses showed a trend favoring AKL-T01 across every outcome measure.

Consistent with the favourable safety profile reported in previous studies, AKL-T01 was shown to be safe in this study, with no serious adverse events observed, suggesting that AKL-T01 could safely be added to the standard of care. All adverse events reported were mild, including frustration (3%) and headache (2%).

"These results build upon the growing body of evidence of AKL-T01's impact on attention and related impairments in children with ADHD," said Dr Anil Jina, Chief Medical Officer at Akili. "Inattention and other underrecognised cognitive impairments can significantly impact daily functioning and quality of life. We're committed to pursuing novel, safe and effective approaches to help those affected."

The *STARS-ADHD* study represents the company's largest clinical trial of AKL-T01 which has to-date been studied across five clinical trials including more than 600 children diagnosed with the disorder. Further researching the clinical implications of the attentional treatment on patients' daily lives, Akili recently conducted the *STARS-ADHD* Adjunctive study evaluating AKL-T01 in children with ADHD when used with and without stimulant medication as well as evaluating the effects of increasing the duration of AKL-T01 treatment. In the *STARS-ADHD* Adjunctive study, AKL-T01 showed a statistically significant improvement in the IRS when used alone and as adjunct to stimulants, and parents and clinicians saw increased improvements with a longer duration of AKL-T01 treatment (nearly 70% saw improvements after two months of treatment). Additional studies of AKL-T01 are underway, including a study to measure frontal-midline theta (MFT) power through electroencephalogram (EEG) in children with ADHD before and after treatment with AKL-T01.

About AKL-T01 and *STARS-ADHD*

AKL-T01 is a digital therapeutic being evaluated as a potential treatment for inattention in children living with ADHD. AKL-T01 is built on Akili's Selective Stimulus Management engine (SSME™) core technology, which presents a range of specific stimuli designed to target and activate the fronto-parietal network in the brain, known to play a key role in cognitive function and attention. SSME has been shown to improve measures of attention in a dozen different indications and has been studied in more than 30 clinical trials. The treatment is delivered through a captivating action video game to help drive engagement and compliance. Akili filed for clearance of AKL-T01 for the treatment of children with ADHD with the United States Food and Drug Administration (FDA) in 2018. Clearance has not yet been granted, and Akili continues to work with FDA in an effort to make the product available for children living with ADHD as soon as possible.

The *STARS-ADHD* pivotal study of AKL-T01 was a randomised, double-blind, active-controlled study conducted across 20 sites. The study enrolled 348 children and adolescents ages 8-12 diagnosed with ADHD. Patients were randomised 1:1 to AKL-T01 or an active control. Both groups used the treatment/control at home on a tablet device for four weeks. The control application was deployed in the same format as AKL-T01, a mobile tablet, mimicked the reward and engagement of AKL-T01, and had an expectation of benefit equivalent to AKL-T01. After the four-week period, an in-clinic assessment measured changes from baseline. The primary endpoint of the study was change in the Attention Performance Index (API), a composite score from the Test of Variables of Attention (T.O.V.A.®), an FDA-cleared continuous performance test measuring sustained attention and inhibitory control. Secondary outcomes included subjective parent- and clinician-reported behavioral ratings. The study was managed by Duke Clinical Research Institute.

About TOVA, IRS and ADHD-RS

The Test of Variables of Attention (T.O.V.A.®) is an objective FDA-cleared continuous performance test that measures the key components of attention and inhibitory control. The T.O.V.A.® is used by qualified healthcare professionals as an aid in the assessment of attention deficits, including attention-deficit/hyperactivity disorder (ADHD), in children and adults.

The Impairment Rating Scale (IRS) is a parent-reported scale of ADHD-specific impairment across domains such as social functioning, academic progress and self-esteem, including an overall impairment rating. The domains of ADHD-specific impairment assessed by the IRS correspond to DSM criteria of impaired functioning in social or academic areas for ADHD. The assessment provides measures of real-world consequences of ADHD symptoms.

The ADHD Rating Scale (ADHD-RS) obtains parent ratings regarding the frequency of ADHD symptoms based on DSM-IV criteria. Parents are asked to determine symptomatic frequency that describes the child's home behavior. The scale consists of two subscales: inattention and hyperactivity-impulsivity.

About Akili

Akili is combining scientific and clinical rigour with the ingenuity of the tech and entertainment industries to challenge the status quo of medicine. Akili is pioneering the development of digital treatments and care solutions to help people affected by cognitive impairments. Akili's treatments are designed to directly activate the networks in the brain responsible for cognitive function and have been rigourously tested in extensive clinical studies, including prospective randomised, controlled trials. Driven by Akili's belief that effective medicine can also be fun and engaging, Akili's treatments are delivered through captivating action video game experiences. For more information, please visit www.akiliinteractive.com.

About PureTech Health

PureTech is a clinical stage biotechnology company dedicated to discovering, developing and commercialising highly differentiated medicines for devastating diseases, including intractable cancers, lymphatic and gastrointestinal diseases, central nervous system disorders, and inflammatory and immunological diseases, among others. The Company has created a broad and deep pipeline through the expertise of its experienced research and development team and its extensive network of scientists, clinicians and industry leaders. This pipeline, which is being advanced both internally and through PureTech's affiliates, is comprised of 23 product candidates and one product that has been cleared by the US Food and Drug Administration (FDA). All of the underlying programmes and platforms that resulted in this pipeline of product candidates were initially identified or discovered and

then advanced by the PureTech team through key validation points based on the Company’s unique insights into the biology of the brain, immune, and gut, or BIG, systems and the interface between those systems, referred to as the BIG Axis. For more information, visit www.puretechhealth.com or connect with us on Twitter @puretechh.

Forward Looking Statement

This press release contains statements that are or may be forward-looking statements, including statements that relate to the company's future prospects, developments, and strategies. The forward looking statements are based on current expectations and are subject to known and unknown risks and uncertainties that could cause actual results, performance and achievements to differ materially from current expectations, including, but not limited to, those risks and uncertainties described in the risk factors included in the regulatory filings for PureTech Health plc. These forward-looking statements are based on assumptions regarding the present and future business strategies of the company and the environment in which it will operate in the future. Each forward-looking statement speaks only as at the date of this press release. Except as required by law and regulatory requirements, neither the company nor any other party intends to update or revise these forward-looking statements, whether as a result of new information, future events or otherwise.